USDA-ARS/
U.S. Wheat and Barley Scab Initiative
FY15 Final Performance Report
Due date: July 15, 2016

Cover Page

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Fiscal Year:	2015
USDA-ARS Agreement ID:	59-0206-4-008
USDA-ARS Agreement Title:	Application of Hormonal Biomarkers for DON-3-Glucoside Risk Assessment.
FY15 USDA-ARS Award Amount:	$ 67,325
Recipient Organization:	Michigan State University Contract & Grant Administration Hannah Administration Building, Room 2 East Lansing, MI 48824-1046
DUNS Number:	193247145
EIN:	38-6005984
Recipient Identifying Number or Account Number:	RC103734
Project/Grant Reporting Period:	05/03/15-05/02/16
Reporting Period End Date:	05/02/16

USWBSI Individual Project(s)

USWBSI Research Category*	Project Title	ARS Award Amount
FST-R	Hormonal Biomarkers for Trichothecene Risk Assessment.	$ 67,325
	FY15 Total ARS Award Amount	**$ 67,325**

7-6-16

Principal Investigator Date

* MGMT – FHB Management
FST – Food Safety & Toxicology
GDER – Gene Discovery & Engineering Resistance
PBG – Pathogen Biology & Genetics
EC-HQ – Executive Committee-Headquarters
BAR-CP – Barley Coordinated Project
DUR-CP – Durum Coordinated Project
HWW-CP – Hard Winter Wheat Coordinated Project
VDHR – Variety Development & Uniform Nurseries – Sub categories are below:
SPR – Spring Wheat Region
NWW – Northern Soft Winter Wheat Region
SWW – Southern Soft Red Winter Wheat Region

Project 1: *Hormonal Biomarkers for Trichothecene Risk Assessment.*

1. What are the major goals and objectives of the project?

The toxic endpoints used to set regulatory standards for DON are growth retardation and emesis. The FDA has established a 1 ppm level of concern for DON in flour. These levels are in concurrence with Japanese, Canadian, and Russian standards. In contrast, the European Union has established regulatory limits for DON of 200 and 500-750 ppb for infant and adult foods, respectively. There are two important considerations concerning these standards. First, a 100 fold uncertainty factor had already been applied to the No Observed Adverse Effect Level (NOAEL) in mice to achieve the tolerable daily intake on which the 1 ppm estimates were derived. Second, the EU used an extremely conservative exposure estimate based on 95% maximum likelihood estimate of a probabilistic model. Currently, there is active discussion by CODEX on how to best harmonize regulations for DON and its congeners. Several research studies suggest these effects are mediated by neuroendocrine hormones. Thus any evaluation of DON-3-G toxicity should include measurement of these responses. Enteroendocrine cells (EECs) are one of the four primary intestinal cell subtypes that populate the epithelial layer of the GI tract. EEC normally sense the contents of the gut lumen and respond by secreting a range of peptide and amine hormones that can act on adjacent cells, afferent enteric neurons and more distal cells. These hormones control numerous digestive and physiologic functions. We tested the guiding hypothesis that DON and DON-3-G differentially regulate hormone secretion EEC models from mice and mink. Our research is critical because it will help discern whether DON-3-G is sufficiently toxic to include in the TDI for DON. The resulting data will be applicable to DON safety assessments and enable determination of the accuracy of existing hazard data being used for establishing international guidelines.

2. What was accomplished under these goals?

Accomplishment: We have compared the anorectic effects of DON-3-G and DON in the mouse. While the thresholds and kinetics of the response were different, the effects of DON-3-G and DON were similar.
Outcome: Using food refusal in mice as an endpoint, it might be appropriate to include DON-3-G with DON in safety assessment from chronic exposures

Accomplishment: We have compared the inflammatory effects of DON-3-G and DON in the mouse and found DON-3-G was largely incapable of inducing proinflammatory cytokine expression
Outcome: In risk assessments of acute inflammatory effects of DON, it is not appropriate to include DON-3-G.

Accomplishment: We have compared the emetic effects of DON-3-G and DON in the mink and found DON-3-G was 40x less effective than DON causing vomiting
Outcome: In risk assessments of acute emetic effects of DON, it is not appropriate to include DON-3-G.

3. What opportunities for training and professional development has the project provided?

Training experiences included designing experiments, conducting lab analyses, taking courses in food science/toxicology courses, one-on-one mentoring, presenting research at meetings and writing/submitting research manuscripts.

4. How have the results been disseminated to communities of interest?

We have presented our research at local, national and international meetings. We have published our findings in international public journals with high impact factors.

Paul Schwartz and I presented a Webinar on Fusarium Head Blight & Craft Malt to the Craft Maltsters Guild in October 2015.

Training of Next Generation Scientists

Instructions: Please answer the following questions as it pertains to the FY15 award period. The term "support" below includes any level of benefit to the student, ranging from full stipend plus tuition to the situation where the student's stipend was paid from other funds, but who learned how to rate scab in a misted nursery paid for by the USWBSI, and anything in between.

1. **Did any graduate students in your research program supported by funding from your USWBSI grant earn their MS degree during the FY15 award period?**
   No
   If yes, how many?

2. **Did any graduate students in your research program supported by funding from your USWBSI grant earn their Ph.D. degree during the FY15 award period?**
   Yes
   If yes, how many?
   One, Erica Clark. She has been hired as a Principal Scientist by FDA.

3. **Have any post docs who worked for you during the FY15 award period and were supported by funding from your USWBSI grant taken faculty positions with universities?**
   Yes
   If yes, how many?
   One, Wenda Wu. He is now an Assistant Professor at University of Nanking Veterinary School.

4. **Have any post docs who worked for you during the FY15 award period and were supported by funding from your USWBSI grant gone on to take positions with private ag-related companies or federal agencies?**
   No
   If yes, how many?

Release of Germplasm/Cultivars

Instructions: In the table below, list all germplasm and/or cultivars released with full or partial support through the USWBSI during the FY15 award period. All columns must be completed for each listed germplasm/cultivar. Use the key below the table for Grain Class abbreviations. *Leave blank if you have nothing to report or if your grant did NOT include any VDHR-related projects.*

Name of Germplasm/Cultivar	**Grain Class**	**FHB Resistance** (S, MS, MR, R, where R represents your most resistant check)	**FHB Rating** (0-9)	**Year Released**

Add rows if needed.

NOTE: List the associated release notice or publication under the appropriate sub-section in the 'Publications' section of the FPR.

Abbreviations for Grain Classes

Barley - BAR
Durum - DUR
Hard Red Winter - HRW
Hard White Winter - HWW
Hard Red Spring - HRS
Soft Red Winter - SRW
Soft White Winter - SWW

Publications, Conference Papers, and Presentations

Refer to the FY15-FPR_Instructions for listing publications/presentations about your work that resulted from all of the projects included in the FY15 grant. If you did not have any publications or presentations, state 'Nothing to Report' directly above the Journal publications section.

Journal publications.

Clark, E.S., Flannery, B.M., Gardner, E.M., Pestka, J.J. (2015) High sensitivity of aged mice to deoxynivalenol (vomitoxin)-induced anorexia corresponds to elevated proinflammatory cytokine and satiety hormone responses. *Toxins*, 7 (10), 4199-4215.
Status: Published
Acknowledgement of Funding Support: Yes

Clark, E.S., Flannery, B.M., Pestka, J.J. (2015) Murine anorectic response to deoxynivalenol (vomitoxin) is sex-dependent. *Toxins*, 7 (8), 2845-2859.
Status: Published
Acknowledgement of Funding Support: Yes

Wu, W., Zhou, H.R., Pan, X., Pestka, J.J. (2015) Comparison of anorectic potencies of the trichothecenes T-2 toxin, HT-2 toxin and satratoxin g to the ipecac alkaloid emetine. *Toxicol Rep*, 2 (238-251.
Status: Published
Acknowledgement of Funding Support: Yes

Zhou, H.R., Pestka, J.J. (2015) Deoxynivalenol (vomitoxin)-induced cholecystokinin and glucagon-like peptide-1 release in the STC-1 enteroendocrine cell model is mediated by calcium-sensing receptor and transient receptor potential ankyrin-1 channel. *Toxicological Sciences*, 145 (2), 407-417.
Status: Published
Acknowledgement of Funding Support: Yes

Male, D., Wu, W., Mitchell, N.J., Bursian, S., Pestka, J.J., Wu, F. (2016) Modeling the emetic potencies of food-borne trichothecenes by benchmark dose methodology. *Food Chem Toxicol*, 94 (178-185.
Status: Published
Acknowledgement of Funding Support: Yes

Wu, W., Zhou, H.R., Bursian, S.J., Link, J.E., Pestka, J.J. (2016) Emetic responses to t-2 toxin, ht-2 toxin and emetine correspond to plasma elevations of peptide yy3-36 and 5-hydroxytryptamine. *Archives of Toxicology*, 90 (4), 997-1007
Status: Published
Acknowledgement of Funding Support: Yes

Wu, W., Zhou, H.R., Pestka, J.J. (2016) Potential roles for calcium-sensing receptor (casr) and transient receptor potential ankyrin-1 (trpa1) in murine anorectic response to deoxynivalenol (vomitoxin). *Archives of Toxicology*, (in press).
Status: In Press
Acknowledgement of Funding Support: Yes

Books or other non-periodical, one-time publications.

Other publications, conference papers and presentations.

Pestka, J.J. (July 24, 2015) *Prediction and Mitigation of Foodborne Disease Potential of Emerging Trichothecene Mycotoxins.* USDA NIFA Food Safety Project Directors' Meeting, Portland, Oregon.
Status: Presented
Acknowledgement of Funding Support: Yes

Pestka, J.J., and Schwarz, P. (Oct, 28, 2015). *Fusarium Head Blight & Craft Malt.* Webinar to Craft Maltsters Guild.
Status: Presented
Acknowledgement of Funding Support: Yes